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Metaprogramming and Genomics

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Abstract

V(D)J (Variable, Diversity, and Joining segments) recombination allows the genome to encode millions of immunoglobulin proteins using a small number of germ-line DNA segments. Immune cells can rearrange these segments into millions of sequences, which are then used as templates for proteins. As opposed to alternative splicing, the DNA physically rearranges itself during cell maturation (Market and Papvasiliou 2003). This is similar to the behavior of metaprograms in computer science which perform source code rearrangements before compilation. The proteins which cut and rearrange the template DNA is a metaprogramming system, and the DNA sequence that is rearranged is a metaprogram.

Metaprogramming is a computer programming technique where a specialized programming language is defined in which programs written in this language are translated into an already-existing language, where the specialized language only contains constructs that apply to specific sets of tasks. This allows the programmer to operate directly on specifications, while the complexities of integrating those specifications together are in the metaprogramming system. The metaprogramming system is tasked with keeping the metaprogramming rearrangements meaningful and consistent (Bartlett 2005).

Similarly, genetic codes for V(D)J segments do not have to rely on specific knowledge of the interactions, just of the basic specifications. The metaprogramming system is responsible for integrating the specifications in a way that functions properly. This allows for complex integrations using simple components. In mice, for instance, arginine is essential at the V/J intersection, but not all combinations of V/J segments would generate an arginine based on the segment sequences alone. However, the recombination mechanism can generate the needed arginine if neither the V nor J codes for it (Sanz and Capra 1987). Thus, the metaprogramming system is "smart" in that the interactions between components are taken care of by the metaprogramming system.

Recently, the addition of N and P (non-templated and palindromic) elements and nucleotide deletions at the junction of segments has been detected, and is non-random (Gauss and Lieber 1996). According to the metaprogramming model it is predicted that the constraints they follow use a similar pattern of "smart" joining, with the changes oc-

curring for structural or other functional considerations. This allows hypermutation of segment regions without adversely affecting the final immunoglobulin's integrity.

A new type of metaprogramming, termed "enterprise metaprogramming", allows a single metaprogram to serve for multiple related metaprogramming systems. For example, a single metaprogram describing data entities may be read by separate metaprogramming systems to generate a database design, a C++ class specification, and a data-entry tool, each integrating with the other (Bartlett 2006).

This author recommends that biologists watch for such multi-system metaprograms in the genome, characterized by a DNA template sequence which would be recombined in multiple ways for multiple, interacting subsystems; such that the organism's metaprogramming system would cause a change at one locus to affect multiple systems, perhaps in different but related tissues. The metaprogram would act as a multisystem specification, and each differentiated tissue would act on that specification in unique ways, resulting in uniquely recombined DNA that worked together system-wide.

References

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